REMARKS

The foregoing amendments and the following remarks are submitted in response to the Office Action dated November 18, 2008. Applicants respectfully request entry and acceptance of the amendments and remarks herein.

Applicants acknowledge and thank the Examiner for her time and consideration in telephone discussion on January 27, 2009 in which the outstanding rejections were discussed. In particular, the 102 reference Fischetti et al was discussed and various aspects of the present invention which Applicants allege distinguish over Fischetti et al. The 112, first paragraph rejections, were also discussed, including the teaching in the specification, common characteristics of gram-positive bacteria, and further studies evidencing glycosylated endopeptidase enzymes. The double patenting advisement and claim amendments and cancellations to address it were discussed.

Status of the Claims

Claims 1, 5-7 and 11-33 are pending in the application. Claims 6 and 34 have been cancelled without prejudice. Claims 1, 5, 7 and 33 have been amended without prejudice including to clarify the invention. Withdrawn process claim 12 remains and depends from and thereby requires all the limitations of the product claim (claim 1). Support for the amendments can be found throughout the specification and in the original and previously presented claims. In particular, support for the language of claims 1 and 33 wherein the carbohydrates "are linked to the polypeptide backbone" can be found generally in the specification, including at page 3, paragraph [0008], and at page 28, paragraph [0096]. No new matter has been added by way of these amendments. Thus, as a result of the foregoing amendment, claims 1, 5, 7, 28, 29 and 33 are under consideration. Reconsideration of this application and allowance of the claims is respectfully requested. Applicants request rejoinder of method claim 12 with the allowable product claims.

With respect to all amendments and canceled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and, moreover, has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Rejections under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 33 and 34 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner alleges and states that the claims recite an enzyme having any possible activity from any possible specie of the genera *Staphylococcus* or *Streptococcus* that possess the properties that are recited in the claims, further remarking that "despite the claimed properties, the activity of the enzyme is not identified. In addition and similarly, Claims 1 and 28 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. With regard to claims 1 and 28, the Examiner alleges that the claims recite an endopeptidase isolated from any possible specie of the genera *Staphylococcus* or *Streptococcus* that possess the properties that are recited in claim 1.

Applicants respectfully traverse the Examiner's rejections of each and all of claims 33, 34, 1, and 28 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The following arguments and response applies to these 112, first paragraph rejections collectively. Applicants point out that claim 34 has now been cancelled rendering the rejection of this claim moot. Applicants submit that claims 1, 28, and 33 each and all meet the requirements of 35 U.S.C. §112, first paragraph, including with regard to written description. The Examiner alleges that the rejected claims encompass any enzyme with any possible activity isolated from any possible source of *Staphylococcus* or *Streptococcus* that has this claimed characteristics for which no specific written description has been provided. Applicants underscore that the claimed glycosylated enzyme is isolated from *Streptococcus* or *Staphylococcus* and uniquely possesses a series of recited and specific characteristics and activities, which particularly describe and distinguish the enzyme. In addition, the specification describes methods for the isolation of the enzyme and demonstrates its isolation from both *Streptococcus* and *Staphylococcus* sources. Applicants assert that other *Staphylococcus* and *Streptococcus* sources for the enzyme are clearly contemplated and fully expected, including as evidenced in the specification and given the knowledge of the skilled artisan at the time of filing.

Underscoring this, Applicants refer to the specification, where at pages 39-40, paragraph [0127], it is established that the purified and specific LPXTGase inhibitor was tested and shown to be effective against various strains, including *S. epidermidis, S. gordonii, S.mutans* and *S. sanguis.*

To further establish that the instant claims comply with the written description requirement and that one of skill in the art would recognize that the inventors had possession of the claimed invention at the time of filing, Applicants submit herewith a declaration by named inventor and renowned bacterial scientist Vincent A. Fischetti. The enclosed declaration underscores that, given the teaching in the specification and their knowledge and understanding of the art, one skilled in the art would predict the existence and ready isolation of the claimed LPXTGase from any of gram-positive bacteria, including any *Streptococcus* and *Staphylococcus* specie or sources. Further, Dr. Fischetti has isolated LPXTGase (glycosylated endopeptidase) from *Streptococcus pneumoniae*, using the methods described in the specification. The *S. pneumoniae* LPXTGase has the activity and characteristics of the claimed glycosylated endopeptidase.

For at least the reasons detailed above, Applicants submit that claims that claims 1, 28, and 33 each and all meet the requirements of 35 U.S.C. §112, first paragraph. Based on the foregoing amendments and remarks, withdrawal of the rejections under 35 U.S.C. §112, first paragraph, and allowance of the claims is respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

Claims 1, 5-7, 28, 29, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claims 1, 33 and 34 are rejected as being incomplete for omitting essential structural cooperative relationships of elements. Claims 5-7, 28, and 29 are included in the rejection as being dependent on rejected claims. The Examiner remarks that it is unclear whether the carbohydrates are complexed with the enzyme, covalently bound to the enzyme, or are part of the substitute. Applicants point out that claims 6 and 34 have now been cancelled, making this rejection moot as to those claims. Applicants underscore that claims 1 and 33 refer particularly to a "glycosylated" enzyme which is recognized in the art as having carbohydrates linked to the enzyme polypeptide. Nonetheless, and without prejudice, Applicants have above amended claims 1 and 33 to clarify the language thereof and state that the carbohydrates "are linked to the polypeptide backbone". Applicants respectfully submit that pending claims 1, 5, 7, 28, 29 and 33 are clear and definite and meet the requirements of 35 U.S.C. 112, second paragraph. Applicants respectfully request that the 35 U.S.C. 112, second paragraph, rejection be withdrawn.

Double Patenting

The Examiner advises that should claims 5 or 33 be found allowable, claims 6 or 34 respectively, will be objected to under 37 CFR 1.175 as being a substantial duplicate thereof. Applicants have above amended claims 5 and 33 to recite *Staphylococcus pyogenes* or *Staphylococcus aureus* and have cancelled claims 6 and 34 without prejudice as substantial duplicates. Applicants submit that the double patenting rejection is addressed by the above claim amendments and respectfully request the rejection be withdrawn.

Claim Rejections - 35 U.S.C. § 102/103

Claims 1, 5-7, 28, 29, 33 and 34 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fischetti et al (US Patent 5,968,763). Fischetti et al is cited as disclosing an isolated enzyme that cleaves the surface proteins of gram-positive bacteria within the LPXTG motif. The Examiner alleges that, in the absence of evidence to the contrary, the enzyme of Fischetti et al inherently possesses properties that anticipate or render obvious the claimed invention.

Applicants respectfully traverse this rejection. Applicants point out that claims 6 and 34 have been cancelled rendering the rejection of these claims moot. Applicants submit that claims 1, 5, 7, 28, 29 and 33, including as above amended, are not anticipated by or obvious in view of Fischetti et al. To anticipate a claim or to establish obviousness a prior art reference must teach or suggest each and every element and limitation of the claim. Fischetti et al does not teach, nor does it suggest, each and every element of pending claims 1, 5, 7, 28, 29 and 33, including as above amended. Applicants point out that the enzyme isolated and described in the Fischetti et al reference is now known and recognized as sortase. Sortase is factually established to be absolutely distinct from the instant claimed glysosylated endopeptidase enzyme (LPXTGase). In particular, and as previously argued, Applicants underscore that sortase cleaves the LPXTG motif at a different amino acid position, after the threonine, whereas the instant LPXTGase (glycosylated endopeptidase) cleaves the LPXTG motif at a different position, even as set out in the rejected claims, and has a catalytic activity that is 100 times greater than sortase.

Taking the Fischetti et al reference more generally, Applicants point out that, even in the absence of any knowledge or available facts regarding sortase, which nonetheless did exist at the time of filing, the disclosure of Fischetti et al does not teach or suggest the instant LPXTGase (glycosylated endopeptidase). Applicants underscore that the LPXTGases of the present invention are a wholly novel class of enzymes. The glycosylated endopeptidases of the invention are comprised of uncommon amino acids, have no aromatic amino acids, and comprise D amino acids, indicating that they are assembled enzymatically and are not ribosomally assembled (see page 3, paragraphs [0008] and [0009] of the specification). Fischetti et al clearly anticipates a traditional genetically encoded and ribosomally assembled enzyme, as evidence in its specification, including at column 6, wherein the DNA encoding the cleavage enzyme is described as an aspect of the Fischetti invention and the isolation thereof using well known recombinant DNA technology is clearly contemplated.

Further, and importantly, the Fischetti et al enzyme's activity is enhanced in the presence of DTT, indicating that the enzyme is sulfhydryl dependent (see Example 4, column 14, line 60 to column 15 line 5). At lines 4-5 of column 15, the Fischetti 5,968,763 patent states: "*These results indicate that the enzyme is sulfhydryl dependant.*" We note that this is now a well known and art-recognized characteristic of sortase. Importantly and distinctly, the instant LPXTGase does not contain cysteine and is, therefore, not sulfhydryl dependent. This is evidenced and described in the specification, including at page 10, paragraph [0042], where it states:

> **[0042]** A novel enzyme, designated "LPXTGase" has been identified and isolated from cell membrane extracts of *Streptococcus pyogenes.* This enzyme possesses endopeptidase activity and cleaves a conserved LPXTG (SEQ ID NO:1) motif present in surface proteins on gram positive bacteria. LPXTGase, which is about 14,000 Da in size, is heavily glycosylated, and its amino acid composition and sequence analysis reveal the absence of aromatic amino acids. Moreover, LPXTGase cleaves after glutamic acid, does not have cysteine or methionine, is totally insensitive to sulfhydryl agents and its activity is inhibited by hydroxylamine. The carbohydrate moiety in LPXTGase appears to be essential for enzyme activity. No precedent for a glycosylated enzyme existing in prokaryotes is known to the inventors.

Applicants point out that each of independent claims 1 and 33 have been above amended, without prejudice and for clarity, to include the recitation "as having no cysteine", which serves to more fully and particularly describe and distinguish the claimed invention. Applicants submit that claims 1, 5, 7, 28, 29 and 33, including as above amended are not anticipated by and are not obvious from Fischetti et al. Fischetti et al does not teach or even suggest the novel glycosylated endopeptidase enzyme of the instant Application including its described and claimed characteristics.

In view of the foregoing amendments and remarks, withdrawal of the rejections under 35 U.S.C. §102 and/or 103 is respectfully requested.

Fees

No fees are believed to be necessitated by the foregoing amendment and response. However, if this is in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

Conclusion

Applicants believe that the foregoing amendments to the claims and arguments place the application in condition for allowance. Withdrawal of the rejections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 129, to effect a resolution.

Respectfully submitted,

Christine E. Dietzel, Ph.D.
Agent for Applicants
Reg. No. 37,309

KLAUBER & JACKSON, LLC
411 Hackensack Avenue
Hackensack, NJ 07601
Tel: (201) 487-5800